

10-04-02

1621

*Application No.	Filing Date	First Named Inventor	Attorney Docket No.	Responsive to Confirmation No.
09/733,801	12/09/2000	David Kenneth Johnson	Johnson 60/17024	2575

104 TASMAN COURT, • 919-345-0339 • Fax 919-462.8767 • E-mail: biolink_life@yahoo.com
 GARY, NC 27513

4 October, 2002

RECEIVED

OCT 08 2002

TECH CENTER 1600/2900

Paul F. Shaver
 Primary Examiner, Group 1600 – Art Unit 1621
 US Patent and Trademark Office
 Washington, DC 20231

Transmitted by facsimile to (703) 308-4556.

Confirming correspondence transmitted by U.S. Postal Service

EU 238485627 US

Sir:

RE: Application No. 09/733,801
 Filing Date 12/09/2000
 First Named Applicant: David Kenneth Johnson

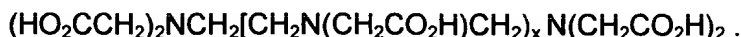
Responsive to the Office Action of 09/09/2002, for which a shortened statutory period for reply was set to expire one month from the mailing date of the communication. Claims 1-21 are pending in this application. Claims 1-21 are subject to restriction and/or election requirement.

1. The restriction is respectfully traversed on the ground that the species of claims 1-21 do not differ substantively in either structure or function and are, therefore, not patentably distinct.

Applicant submits that the species of claims 1-21 are not "organometallic compounds." "Organometallic compounds," by definition, contain at least one covalent bond between a carbon atom and a metal atom.

The chelate-fluorophore tracer species of the present invention are coordination complexes comprising a metal-sequestering agent and a metal ion chelated thereto, said metal-sequestering agent being covalently bonded to a fluorophore. These coordination complexes contain only nitrogen-metal and oxygen-metal bonds.

The structure of each of the metal-sequestering agents of the present invention is based on the structure of the first or second member of a homologous series of synthetic polyamino-polycarboxylate compounds having the general formula:



The common name of the first polyamino-polycarboxylate compound in this homologous series (for which $x = 0$ in the formula above) is ethylenediaminetetraacetic acid (EDTA). The common name of the second polyamino-polycarboxylate compound in this homologous series (for which $x = 1$ in the formula above) is diethylenetriaminepentaacetic acid (DTPA). Both compounds are known in the art to be highly effective metal-sequestering agents, and are known to form very stable metal complexes with a 1:1 stoichiometry. The structural features of the polyamino-polycarboxylate backbone that are responsible for the metal-sequestration abilities of EDTA and

Application No.	Filing Date	First Named Inventor	Attorney Docket No.	Responsive to Confirmation No.
09/733,801	12/09/2000	David Kenneth Johnson	Johnson 60/17024	2575

DTPA (i.e., the amino and carboxylate groups and their positioning on the carbon backbone) are specifically incorporated in the metal-sequestering agents of the present invention to provide stable metal-chelating agent complexes having high thermodynamic stability and 1:1 metal-to-sequestering agent stoichiometry.

Further, a chelate-fluorophore tracer composition of the present invention has an obligatory fluorophore covalently joined to the metal-sequestering agent. The sole function of the fluorophore is to enable the use of fluorescence polarization for the detection and determination of the presence and disposition of the metal ion-sequestering agent complex. Applicant has identified specific fluorophores that are useful in the present invention. To wit, a useful fluorophore-labeled sequestering agent of the present invention, which comprises a fluorophore covalently linked to the metal-sequestering agent, has a fluorescence lifetime and quantum yield suitable for monitoring hapten-antibody binding at nanomolar concentrations.

Applicant also discloses chelate-fluorophore tracer compositions comprising metal-sequestering agents having a covalently joined fluorophore that further and optionally have substituents other than hydrogen attached at the methylene carbon atoms of the polyamine backbone (R_3 and R_4 of the formula in Claim 1). Incorporation of these substituents (CH_3 or a fused ring system) does not alter the metal-sequestering properties of the metal-chelating reagent. Applicant hypothesizes that these substituents may contribute to antigenic determinants recognized by an antibody.

No given combination of metal, metal-sequestering agent, and covalently joined fluorophore performs a substantively different function from any other such combination. Such combinations, therefore, constitute obvious variants of the species elected below.

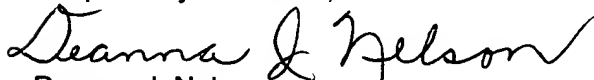
2. Elected for examination is the species of claim 1 wherein:

$m = 0$,
 $R_4 = H$,
 $R_1 = -CH_2C_6H_4-X-Y$,
 $X = -NHC(S)NH-$,
 $Y = \text{fluorescein}$,
 $M = Pb$, and
 $n = 2$.

This is the species of Example 2a of the present invention. This compound has the molecular formula $C_{38}H_{32}N_4O_{13}SPb$, assuming that the net electronic charge of the complex is balanced by protons.

Applicant respectfully requests examination of this Application. Should additional information be required, Deanna J. Nelson is representing Applicant before the Office. She is available by telephone at (919) 345-0339 during the hours of 8:00 AM to 4:00 PM Monday through Friday and by facsimile at (919) 462-8767.

Respectfully submitted,



Deanna J. Nelson
Registration Number 44,968

FAX RECEIVED

OCT 04 2002

GROUP 1600

104 Tasman Court
Cary, NC 27513

Phone: 919.462.8767

Fax: 919.462.8767

Email: dj_nelson_2k@yahoo.com

*Fax Transmittal Form***OFFICIAL**

To

Name: Mr. Paul F. Shaver
Organization Name/Dept: Group 1600
Art Unit 1621
Phone number: (703) 308-4629
Fax number: (703) 308-4556

From

D J Nelson
Phone: 919.462.8767
Fax: 919.462.8767
Email: dj_nelson_2k@yahoo.com

☒ Response to Office Action

Date sent: October 3, 2002
Time sent: 2:10 PM
Number of pages including cover page: 3

Message:

Application No.	Filing Date	First Named Inventor	Attorney Docket No.	Responsive to Confirmation No.
09/733,801	12/09/2000	David Kenneth Johnson	Johnson 60/17024	2575

104 TASMAN COURT, • 919-345-0339 • Fax 919-462.8767 • E-mail: biolink_life@yahoo.com
CARY, NC 27513

4 October, 2002

Mr. Paul F. Shaver
Primary Examiner, Group 1600 – Art Unit 1621
US Patent and Trademark Office
Washington, DC 20231

FAX RECEIVED

OCT 04 2002

GROUP 1600

Transmitted by facsimile to (703) 308-4556.
Confirming correspondence transmitted by U.S. Postal Service

Sir:

RE: Application No. 09/733,801
Filing Date 12/09/2000
First Named Applicant: David Kenneth Johnson

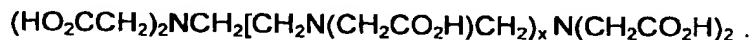
Responsive to the Office Action of 09/09/2002, for which a shortened statutory period for reply was set to expire one month from the mailing date of the communication. Claims 1-21 are pending in this application. Claims 1-21 are subject to restriction and/or election requirement.

1. The restriction is respectfully traversed on the ground that the species of claims 1-21 do not differ substantively in either structure or function and are, therefore, not patentably distinct.

Applicant submits that the species of claims 1-21 are not "organometallic compounds." "Organometallic compounds," by definition, contain at least one covalent bond between a carbon atom and a metal atom.

The chelate-fluorophore tracer species of the present invention are coordination complexes comprising a metal-sequestering agent and a metal ion chelated thereto, said metal-sequestering agent being covalently bonded to a fluorophore. These coordination complexes contain only nitrogen-metal and oxygen-metal bonds.

The structure of each of the metal-sequestering agents of the present invention is based on the structure of the first or second member of a homologous series of synthetic polyamino-polycarboxylate compounds having the general formula:



The common name of the first polyamino-polycarboxylate compound in this homologous series (for which $x = 0$ in the formula above) is ethylenediaminetetraacetic acid (EDTA). The common name of the second polyamino-polycarboxylate compound in this homologous series (for which $x = 1$ in the formula above) is diethylenetriaminepentaacetic acid (DTPA). Both compounds are known in the art to be highly effective metal-sequestering agents, and are known to form very stable metal complexes with a 1:1 stoichiometry. The structural features of the polyamino-polycarboxylate backbone that are responsible for the metal-sequestration abilities of EDTA and

Application No.	Filing Date	First Named Inventor	Attorney Docket No.	Responsive to Confirmation No.
09/733,801	12/09/2000	David Kenneth Johnson	Johnson 60/17024	2575

DTPA (i.e., the amino and carboxylate groups and their positioning on the carbon backbone) are specifically incorporated in the metal-sequestering agents of the present invention to provide stable metal-chelating agent complexes having high thermodynamic stability and 1:1 metal-to-sequestering agent stoichiometry.

Further, a chelate-fluorophore tracer composition of the present invention has an obligatory fluorophore covalently joined to the metal-sequestering agent. The sole function of the fluorophore is to enable the use of fluorescence polarization for the detection and determination of the presence and disposition of the metal ion-sequestering agent complex. Applicant has identified specific fluorophores that are useful in the present invention. To wit, a useful fluorophore-labeled sequestering agent of the present invention, which comprises a fluorophore covalently linked to the metal-sequestering agent, has a fluorescence lifetime and quantum yield suitable for monitoring hapten-antibody binding at nanomolar concentrations.

Applicant also discloses chelate-fluorophore tracer compositions comprising metal-sequestering agents having a covalently joined fluorophore that further and optionally have substituents other than hydrogen attached at the methylene carbon atoms of the polyamine backbone (R_3 and R_4 of the formula in Claim 1). Incorporation of these substituents (CH_3 or a fused ring system) does not alter the metal-sequestering properties of the metal-chelating reagent. Applicant hypothesizes that these substituents may contribute to antigenic determinants recognized by an antibody.

No given combination of metal, metal-sequestering agent, and covalently joined fluorophore performs a substantively different function from any other such combination. Such combinations, therefore, constitute obvious variants of the species elected below.

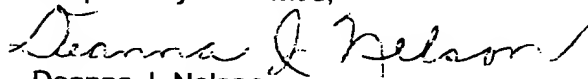
2. Elected for examination is the species of claim 1 wherein:

$m = 0$,
 $R_4 = H$,
 $R_1 = -CH_2C_6H_4-X-Y$,
 $X = -NHC(S)NH-$,
 $Y = \text{fluorescein}$,
 $M = Pb$, and
 $n = 2$.

This is the species of Example 2a of the present invention. This compound has the molecular formula $C_{38}H_{32}N_4O_{13}SPb$, assuming that the net electronic charge of the complex is balanced by protons.

Applicant respectfully requests examination of this Application. Should additional information be required, Deanna J. Nelson is representing Applicant before the Office. She is available by telephone at (919) 345-0339 during the hours of 8:00 AM to 4:00 PM Monday through Friday and by facsimile at (919) 462-8767.

Respectfully submitted,


Deanna J. Nelson
Registration Number 44,968